

REMARKS

Claims 74-168 are pending and claims 109-111, 115-117 and 121-123 are allowed. Claims 74, 83, 84, 106, 118, and 124 have been amended and find basis in the claims as originally filed and in the specification throughout (e.g., original claims 8, 12, 29, 35, paragraphs 0021, 0120, 0123, 0240, 0241, and Examples 1 and 4). Claims 129-166 are new and find basis in the claims as originally filed and in specification throughout (e.g., original claims 8, 12, 29, 35, paragraphs 0021, 0120, 0123, 0240, 0241, and Examples 1 and 4). Accordingly, entry of the new claims and claim amendments will not introduce any prohibited new matter.

The Office rejected claims in the outstanding action as summarized hereafter:

- i. Claims 106-108, 118-120, and 124-128 were rejected under 35 U.S.C. 112, second paragraph as being indefinite;
- ii. Claims 74-83, 85-91, 94-102, 105, 113 and 114 were rejected under 35 U.S.C. 102(b) as being anticipated by Foote;
- iii. Claim 112 was rejected under 35 U.S.C. 103(a) as being obvious over Foote;
- iv. Claims 84, 92, 93, and 104 were rejected under 35 U.S.C. 103(a) as being obvious over Foote in view of Zabeau;
- v. Claim 103 was rejected under 35 U.S.C. 103(a) as being obvious over Foote in view of Muller; and
- vi. Claims 74-123 were provisionally rejected for alleged obviousness-type double patenting over U.S. Application No. 10/933,611.

Applicant respectfully traverses these rejections for the reasons presented hereafter. The claims were amended in order to expedite prosecution, and Applicant respectfully asserts the outstanding rejections are inapplicable to the subject matter claimed herein.

Informality Objection

Claim 124 was objected to for clerical errors. Claim 124 as amended now alleviates these errors. Applicant therefore respectfully requests withdrawal of the objection.

Rejection for alleged indefiniteness

Claims 106-108, 118-120 and 124-128 were rejected under 35 U.S.C. 112, second paragraph for alleged indefiniteness. The rejection respectfully is traversed and is inapplicable to amended claims 106, 118, 124 and their dependent claims in view of the reasoning presented hereafter.

Claims 106 and 118 have been amended to recite “candidate” sequences having at most k sequence variations. Due to clerical errors, “reference” sequence was inadvertently written instead of “candidate” sequence. This amendment finds basis in the claims as originally filed and in the specification throughout (e.g., original claims 8 and 12).

Claim 124, step a, has been amended to recite “the target sequence” and “different fragments between target nucleic acid fragments and reference nucleic acid fragments” to more clearly define the claimed invention.

Accordingly, the outstanding rejections for alleged indefiniteness are inapplicable to amended claims 106, 118, 124 and their dependent claims. Applicant therefore requests withdrawal of outstanding rejections under 35 U.S.C. 112, second paragraph.

Rejection for alleged anticipation and obviousness

Claims 74-83, 85-91, 94-102, 105, 113 and 114 were rejected under 35 U.S.C. 102(b) as they allegedly were anticipated by Foote. Claim 112 was rejected under 35 U.S.C. 103(a) as being obvious over Foote. Claims 84, 92, 93, and 104 were rejected under 35 U.S.C. 103(a) as being obvious over Foote in view of Zabeau and Claim 103 was rejected under 35 U.S.C. 103(a) as being obvious over Foote in view of Muller.

The Office states on page 6 of the action that Foote teaches “carrying out further specific cleavages and integrating the data in order to arrive at the nature and the position of the nucleotide variation.” The Office concludes this passage of Foote “qualifies as identifying a reduced set of sequence variation candidates,” and that Foote identifies a reduced set based on further cleavages of candidate sequences. The rejections respectfully are traversed and Applicant respectfully submits the rejections are inapplicable to the new claims.

Claims 74-114 are directed to methods for determining the sequence of one or more sequence variations in a target nucleic acid, which comprise providing mass signals of

fragments resulting from one specific cleavage of a target nucleic acid and a reference nucleic acid and identifying differences in mass signals between target nucleic acid fragments and reference nucleic acid fragments. One or more compomer witnesses are generated for the different fragments identified, and a reduced set of candidate sequence variations corresponding to the compomer witnesses is produced. The one or more sequence variations in the target nucleic acid are determined from the candidate sequence variations.

Thus, independent claim 74 and its dependent claims specify that a reduced set is based on compomer witnesses from the original cleavage, and not based on further cleavages of candidate sequences as taught by Foote. Support for this feature can be found throughout the instant application (e.g. Figures 1 and 2 and paragraph 0123).

Foote fails to teach or suggest limitations of the claimed processes presented herein, i.e. determining the sequence of one or more sequence variations in a target nucleic acid, providing mass signals of fragments resulting from one specific cleavage of a target nucleic acid, and identifying a reduced set of candidate sequence variations corresponding to the compomer witnesses is produced. Foote uses one cleavage reaction for fingerprinting. Fingerprinting shows changes in mass spectra peaks but does not elucidate the sequence of a variation (e.g. page 11, lines 15-22). When addressing sequence determinations, however, Foote directs the person of ordinary skill in the art to using multiple cleavage reactions. For example, Foote states “[i]n order to optimise the detection of mutations, four separate base specific cleavage reactions have been performed using separated forward and reverse strands and two different base specific reagents,” (Foote, page 19 lines 9-11; emphasis added). Foote further states “[c]onceivably one could increase the power of the technique by using all four base specific reagents on both strands.” Thus, Foote does not disclose, teach or suggest methods for using one cleavage reaction to determine the sequence of a variation, as specified in claim 74.

Foote also does not teach or suggest determining the sequence composition of an unknown sequence as is specified in dependent claim 168. Specifically, Foote states cleavage of two known oligonucleotides 1 and 2 (SEQ ID NO 1 and SEQ ID NO 2) is “sufficient to assign the correct base composition, however, it is not sufficient to blindly assign base composition peaks from a sample of unknown sequence” (page 20, lines 1-2;

emphasis added). Foote therefore teaches away from determining the sequence composition of an unknown sequence using only one cleavage reaction as specified in claim 168.

The other cited documents, Zabeau and Muller, do not cure the deficiencies of Foote. Foote therefore cannot anticipate the claimed invention nor can the cited documents support, alone or in combination, a *prima facie* case of obviousness. Accordingly, Applicant respectfully requests withdrawal of the anticipation and obviousness rejections.

Foote, alone or in combination with the other cited documents, also does not teach or suggest all the limitations of the claimed processes presented in new claim 129 and its dependent claims. Specifically Foote, nor the other cited documents, teach or suggest identifying a reduced set of candidate sequence variations corresponding to the compomer witnesses represented by $C_k := \{ (c[i, j], b[i, j]) : 1 \leq i \leq j \leq \text{length of } s, \text{ and } \text{ord}[i, j] + \#b[i, j] \leq k \}$, where C is a set of all bounded compomers within a string s , $c[i, j]$ is a compomer corresponding to substring $s[i, j]$, $b[i, j]$ is a boundary of the substring $s[i, j]$, and whereby the one or more sequence variations in the target nucleic acid are determined from the candidate sequence variations. Thus the Office should find new claim 129 and its dependents to be allowable subject matter.

Double Patenting Rejection

Claims 74-123 were provisionally rejected for alleged obviousness-type double patenting over U.S. Application No. 10/933,611. Applicant respectfully requests that the Office hold this rejection in abeyance until allowable subject matter is identified in the instant patent application and copending Application No. 10/933,611.

CONCLUSIONS

Applicant respectfully submits all pending claims will be in condition for allowance upon entry of the amendments herein. Applicant respectfully solicits a prompt notification to this effect, and the Examiner is encouraged to contact the undersigned representative (contact information below) to promptly resolve any remaining issues or questions.

In the unlikely event a fee calculation document or other pertinent document is separated from this submission and the Office determines that an extension and/or other relief is required, Applicant petitions for any required relief, including extensions of time, and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. **50-3473**.

Respectfully submitted,

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